UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/248,964 | 02/12/1999 | KAI W. WUCHERPFENNIG | HAR-005 | 9407 |

21323 7590 07/29/2003

TESTA, HURWITZ & THIBEAULT, LLP
HIGH STREET TOWER
125 HIGH STREET
BOSTON, MA 02110

| EXAMINER | |
|---|---|
| VANDERVEGT, FRANCOIS P | |
| ART UNIT | PAPER NUMBER |
| 1644 | |

DATE MAILED: 07/29/2003

34

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/248,964 | WUCHERPFENNIG ET AL. | |
| | Examiner | Art Unit | |
| | F. Pierre VanderVegt | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20,103 and 114-133* is/are pending in the application.

4a) Of the above claim(s) *1-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *103,114-119-133 and 1230* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

This application claims the benefit of the filing date of provisional application 60/075,351 and is a continuation of PCT/US97/14503, which claims the benefit of the filing date of provisional application 60/024,007.

Claims 21-102 and 104-113 have been canceled previously.

Claims 1-20, 103 and 114-133 are currently pending.

Claims **1-20 stand as withdrawn**.

Claims **103 and 114-133 are the subject of examination** in the present Office Action.

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 6, 2002 has been entered.

### *Claim Rejections - 35 USC § 112*

3. Claims 125-127 and 131-133 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

It was previously stated: "Claims 125-127 are not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation of " An MHC Class II fusion protein comprising a heterodimer, wherein the first polypeptide comprises a fusion of an extracellular domain of an MHC Class II alpha chain and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of an extracellular domain of an MHC Class II beta chain and a second coiled-coil dimerization domain; wherein said fusion protein further comprises

a first immunoglobulin Fc domain positioned at the C terminus of one of the first and second polypeptide chains"."

Applicant's arguments filed September 6, 2003 have been fully considered but they are not persuasive.

Applicant contends that the recitation in the claims is supported by the specification at page 12, lines 15-19, page 23, line 16 to page 24, line 28 and in Figure 2. The Examiner respectfully disagrees with Applicant's position. At page 12, lines 11-19, the specification discloses that the MHC extracellular domain is joined to a dimerization domain that is chosen from a coiled-coil **OR** an immunoglobulin heavy or light chain. Equally, lines 25-29 of page 23 disclose that the dimerization domains are chosen from "a leucine zipper domain or an immunoglobulin Fab constant domain." In contrast, claim 125 recites that the immunoglobulin Fc domain is positioned at the C-terminus of the dimerization domain that is recited in base claim 103 as being a coiled-coil. The specification does not disclose the use of the coiled-coil and the immunoglobulin domain together in the same fusion construct and therefore the recitation in the claim is maintained to be new matter.

It was previously stated: "Claims 131-133 are not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation of "A MHC Class II-peptide complex comprising at least one Class II MHC fusion protein comprising a heterodimer..., wherein the first polypeptide comprises a fusion of...an extracellular domain of an MHC Class II alpha chain and ....a flexible molecular linker, and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of ...an extracellular domain of an MHC Class II beta chain and.... a flexible molecular linker, a second coiled-coil dimerization domain; wherein an fc domain is covalently attached to the C' terminus of one of the first and second dimerization domains... and an MHC binding peptide covalently bound to the MHC Class II fusion protein.""

Applicant contends that the recitation in the claims is supported by the specification at page 12, lines 15-19, page 23, line 16 to page 24, line 28 and in Figure 2. The Examiner respectfully disagrees with Applicant's position. At page 12, lines 11-19, the specification discloses that the MHC extracellular domain is joined to a dimerization domain that is chosen from a coiled-coil **OR** an immunoglobulin heavy or light chain. Equally, lines 25-29 of page 23 disclose that the dimerization domains are chosen from "a leucine zipper domain or an immunoglobulin Fab constant domain." In contrast, claim 125 recites that the immunoglobulin Fc domain is positioned at the C-terminus of the dimerization domain that is recited in the claim as being a coiled-coil. The specification does not disclose the use of the coiled-

coil and the immunoglobulin domain together in the same fusion construct and therefore the recitation in the claim is maintained to be new matter.

**The following represent new grounds of objection/rejection. Applicant's arguments to the previous grounds of rejection are addressed as they apply to the new grounds.**

*Sequence Listing*

2. The disclosure is objected to because of the following informalities:

The paper copy and the computer readable form of the Sequence Listing list U.S. Provisional Application 60/024,007 as a priority document. The '007 provisional is not related to Applicant's invention and appears to be cited due to a typographical error. Applicant should submit replacement paper and CRF copies citing U.S. Provisional Application 60/024,077 instead.

Appropriate correction is required.

*Claim Rejections - 35 USC § 112*

4. Claims 114, 115, 118, 119 and 131-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 114, 115, 118 and 119 are indefinite in the recitation of "comprises residues." The claims do not properly set forth what type of residues are comprised and should be amended to recite --amino acid residues--.

Claim 131 is not distinct in reciting "a second coiled-coil dimerization;" in lines 10-11 of the claim. Applicant should amend the claim to recite --dimerization domain--. Dependent claims 132 and 133 are included in this ground of rejection.

*Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 103, 114- 122-123, 128 and 129 are rejected under 35 U.S.C. 102(a) as being anticipated by Scott et al. (J. Exp. Medicine 183:2087-2095 (May 1996)), as evidenced by U.S. Patent No. 5,837,816 to Ciardelli et al.

Scott et al teach a murine IA Class II MHC fusion protein comprising a heterodimer, wherein the first polypeptide comprises a fusion of an extracellular domain of an MHC Class II alpha chain and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of an extracellular domain of an MHC Class II beta chain and a second coiled-coil dimerization domain, as recited in claim 103, (see entire article, especially the Summary). Scott further teaches that human MHC Class HLA-DQ alleles, unlike HLA-DR alleles, are well known in the art to be promiscuous in their pairing behavior and are able to mismatch with HLA-DR chains (page 2087, column 1 in particular). Said fusion protein taught by Scott et al comprises a leucine zipper domain as recited by claim 122, (see entire article, especially the Summary). Scott also teaches said fusion protein further comprising an MHC binding peptide, wherein said peptide is bound to the MHC Class II fusion protein, as recited in claim 129 (see entire article, including page 2091). Claims 114-115 and 118-119 are included because, while Scott does not specifically disclose that the referenced MHC fusion protein comprises residues 5-180 or residues 5-200 of an MHC Class II alpha chain as recited in claims 114-115 or residues 5-185 or residues 5-205 of an MHC Class II beta chain as recited in claims 118-119, Scott teaches on page 2089, column 1, that the MHC Class II molecules were truncated at the transmembrane region. Accordingly, the segment of the MHC molecule utilized by Scott comprises the entire extracellular region and therefore inherently comprises the recited residues. Claim 128 is included because Scott teaches a flexible linker segment between the MHC domain and the dimerization domain that comprises alanine and serine as a majority of the amino acid residues (Figure 1A in particular). Claim 123 is included because the '816 patent teaches that a leucine zipper refers to a repetitive heptad motif containing 4-5 leucine residues (see entire patent including column 1, lines 55-60). The prior art anticipates the claimed invention. Claims 116, 117, 120 and 121 are included because, while Scott teaches that HLA-DR can form DR$\alpha$/DR$\beta$ heterodimers without having to add a dimerization domain, in conditions where DQ $\alpha$ and $\beta$ chains are also present, according to Scott the DQ $\alpha$ and $\beta$ chains are promiscuous and will readily form a heterodimer with DR haplotypes. Accordingly, when DQ $\alpha$ and $\beta$ chains are present and the DR $\alpha$ and $\beta$ chains do not have dimerization domains to direct their preferential combination, DQ/DR heterodimers would be formed.

Applicant argues that the teachings of Scott are not applicable to human MHC studies because Scott teaches that teaches that methods that are successful for creating HLA-DR dimers are not effective for creating IA dimers due to the promiscuity of IA, substantially asserting that Scott teaches away from

applying the method to human MHC. The Examiner respectfully disagrees with Applicant's position. Scott's teachings differentiate only between HLA-DR and IA, but not between IA and HLA-DQ. In fact, as addressed supra, Scott teaches that IA and HLA-DQ are similar in their properties, reasonably suggesting to the artisan that this method disclosed for IA would be applicable to practice on HLA-DQ as well. It is noted that the claims are drawn to all human MHC Class II, including HLA-DQ and not just HLA-DR.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 103, 123 and 124 is rejected under 35 U.S.C. 103(a) as being unpatentable over Scott et al. in view of US Patent No. 5,837, 816 to Ciardelli et al.

Scott has been discussed supra. Scott does not teach that the leucine zipper domain is selected from the group consisting of a Fos and a Jun leucine zipper domain.

The '816 patent teaches that Fos and Jun comprise leucine zipper domains which preferentially form a heterodimer (see entire patent, especially column 4, lines 44-50).

Accordingly, it would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Scott regarding the manufacture of heterodimers of promiscuous MHC domains using linking domains with the teachings of the '816 patent regarding Fos and June leucine zipper domains. One would have been motivated with a reasonable

expectation of success by the need to produce large quantities of human MHC Class II heterodimers for the study of immune recognition (Scott, Abstract in particular), the teaching of Scott that some human Class II haplotypes are promiscuous in the formation of heterodimers in a manner similar to murine IA haplotypes which can be joined by leucine zippers (page 2087 in particular) and the teaching of the '816 patent that Fos and Jun leucine zipper domains preferentially form a heterodimer which allows the formation of heterodimers of ectodomains with an affinity approaching the comparable cell surface complex (Abstract in particular).

7. Claims 103 and 130 is rejected under 35 U.S.C. 103(a) as being unpatentable over Scott et al. in view of US Patent No. 6,015,884 to Schneck et al.

Scott has been discussed supra. Scott does not teach that the MHC binding peptide is covalently bound to the MHC class II fusion protein.

The '884 patent teaches the covalent linkage of an MHC peptide to a soluble Class II heterodimer (see entire patent, especially Figure 1C) and that said heterodimer has potential use as an immune modulating agent (see entire patent, especially column 5, lines 29-32).

Accordingly, it would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Scott regarding the manufacture of heterodimers of promiscuous MHC domains using linking domains with the teachings of the '884 patent regarding the covalent linkage of an MHC peptide to a soluble Class II heterodimer. One would have been motivated, with a reasonable expectation of success, by the need to produce large quantities of human MHC Class II heterodimers for the study of immune recognition (Scott, Abstract in particular), the teaching of Scott that some human Class II haplotypes are promiscuous in the formation of heterodimers in a manner similar to murine IA haplotypes which can be joined by leucine zippers (page 2087 in particular) in order to study the interaction of the heterodimer with the MHC binding peptide in solution, for example by X-ray crystallography (Scott, page 2094 in particular).

***Conclusion***

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (703) 305-4441. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
July 28, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
7/28/03